CLAIMS

1. A device for extracorporeal purification of mammalian biological fluid such as blood and plasma comprising:

a bioreactor having inlet and outlet ports for, respectively, ingress and egress of biological fluid; inlet and outlet ports for, respectively, ingress and egress of culture medium; and, at least one semi-permeable membrane extending therethrough, which membrane defines a first conduit for ingress and egress of biological fluid and a second conduit for ingress and egress of culture medium;

a mixing vessel in fluid communication with the second conduit, wherein the mixing vessel has an inlet port for introduction of living, unattached hepatocytes into the culture medium;

oxygenation means in gaseous communication with the mixing vessel;

pump means for circulation of biological fluid through the first conduit of the bioreactor; and,

pump means for circulation of hepatocytes and culture medium in the mixing vessel and through the second conduit of the bioreactor.

2. The device according to Claim 1 further comprising at least a theoretical minimum number of unattached hepatocytes.

3. The device according to Claim 1 wherein additional means for removal therefrom of substances selected from the group consisting of antibodies, toxic substances and metabolic waste products are connected to, and in fluid communication with, the

additional means for removal of solutes including antibodies, toxic substances and metabolic waste products, are connected [illegible]

communication with, the bioreactor.

5. The device according to Claim 3 or 4 wherein the additional means comprise one or more means selected from the group consisting of adsorbent means, conventional dialysis means, immunoreactive procedures and hemofiltration.

6. The device according to Claim 1 wherein the semi-permeable membrane is a hollow fiber in which the first conduit is the lumen within the fiber and the second conduit is the space outside of the fiber.

7. The device according to Claim 1 wherein the biological fluid loop is composed of material compatible with fluids selected from the group consisting of blood, plasma and plasma containing plasma extenders.

8. The device according to Claim 1 wherein the living hepatocytes are isolated from liver tissue of pigs.

9. The device according to Claim 1 wherein the living hepatocytes are isolated from liver tissue of humans.

10. The device according to Claim 1 wherein the pump means for circulation of biological fluid through the bioreactor includes a boundary layer pump for movement of the biological fluid through the first conduit of the bioreactor.

11. A device according to Claim 6 wherein the pump means for circulation of biological fluid through the bioreactor includes at least one conduit situated coaxially through hollow fiber semipermeable membranes through which the fluid is circulated by centripetal force.

[illegible] proteins to serve as a barrier for diffusion thereof into the cell culture medium.

13. The device according to [illegible]

means for circulation of the biological fluid include a pump to generate a counterflow for back diffusion of the plasma proteins into the biological fluid.

14. The device according to Claim 1 wherein the semi-permeable membrane is impermeable to proteins.

15. The device according to Claim 1 wherein the semi-permeable membrane is at least partially permeable to proteins.

16. A method for extracorporeal purification of a biological fluid such as blood and plasma, the method comprising:

introduction of at least a theoretical minimum number of living, unattached hepatocytes into a mixing vessel, wherein the mixing vessel is filled with culture medium and is free of air;

circulation of the biological fluid through the bioreactor; and,

circulation of the hepatocytes and culture medium in and from the mixing vessel through a bioreactor having at least one semipermeable membrane passing therethrough, wherein the membrane separates the culture medium from the biological fluid but allows solutes to pass from the biological fluid into the culture medium.

17. The method according to Claim 16 wherein the biological fluid is circulated through the bioreactor at a flow rate of about 20 to 250 milliliters/minute.

18. The method according to Claim 16 wherein the culture medium containing the hepatocytes is circulated through the bioreactor at a flow rate of about 20 to 80 milliliters/minute.

19. The method according to Claim 16 wherein the [illegible] about 6 hours.

20. The method according to Claim 16 wherein all or a portion of the hepatocytes and [illegible]

replaced at least once during the circulation period.

21. The method according to Claim 16 wherein the biological fluid and culture medium are maintained at about the body temperature of the mammal from whom the biological fluid was derived.

22. The method according to Claim 16 wherein antibodies, and/or toxic substances are removed from the biological fluid by additional purification means.

23. The method according to Claim 16 wherein metabolic waste products are removed from the culture medium by additional purification means.

24. A method according to Claim 16 wherein the semi-permeable membrane is impermeable to proteins.

25. A method according to Claim 16 wherein the semi-permeable membrane is at least partially permeable to proteins.

26. A device for extracorporeal purification of mammalian biological fluid such as blood and plasma comprising:

a bioreactor having inlet and outlet ports for, respectively, ingress and egress of biological fluid; inlet and outlet ports for, respectively, ingress and egress of culture medium; and at least one semi-permeable membrane extending therethrough, which membrane defines a first conduit for ingress and egress of biological fluid and a second conduit for ingress and egress of culture medium;

a port in fluid communication with the second conduit for introduction of living hepatocytes attached to a substrate into the culture medium;

pump means for circulation of biological fluid

culture medium into and through the second conduit of the bioreactor.

The device

comprising at least a theoretical minimum number of attached hepatocytes.

28. The device according to Claim 27 wherein at least a portion of the hepatocytes are attached to a metal containing substrate.

29. The device according to Claim 28 further comprising means for generating an alternating magnetic field wherein the field will cause the metal containing substrate to be circulated within the bioreactor.

30. The device according to Claim 27 further comprising additional purification means for removal of antibodies and/or toxic substances from the biological fluid.

31. The device according to Claim 27 further comprising additional purification means for removal of metabolic waste substances from the culture medium.

32. The device according to Claim 27 wherein the living hepatocytes are isolated from liver tissue of pigs.

33. The device according to Claim 27 wherein the living hepatocytes are isolated from liver tissue of humans.

34. The device according to Claim 27 wherein the pump means for circulation of biological fluid through the bioreactor includes a boundary layer pump for movement of the fluid through the first conduit.

35. The device according to Claim 27 wherein the semi-permeable membranes include membranes impermeable to plasma proteins to serve as a barrier for diffusion thereof into the cell culture medium

a pump to generate a counterflow for back diffusion of the plasma proteins into the biological fluid.

37. The device according to Claim

semi-permeable membrane is impermeable to proteins.

38. The device according to Claim 27 wherein the semi-permeable membrane is at least partially permeable to proteins.

39. The device according to Claim 27 wherein the substrate comprises microcarrier particles.

40. The device according to Claim 39 wherein the particles are collagen-coated beads.

41. A method for extracorporeal purification of a biological fluid such as blood and plasma, the method comprising:

introduction of at least a theoretical minimum number of living hepatocytes into a first conduit of a bioreactor;

circulation of the biological fluid through a second conduit of the bioreactor, wherein the first and second conduits are separated by a semi-permeable membrane; and,

circulation of the hepatocytes in the first conduit of the bioreactor.

42. The method according to Claim 41, wherein the hepatocytes are unattached.

43. The method according to Claim 41, wherein the hepatocytes are attached.